(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 July 2004 (22.07.2004)

PCT

(10) International Publication Number
WO 2004/061082 A3

(51) International Patent Classification[7]: C12Q 1/68, C07H /

(21) International Application Number: PCT/US2003/041127

(22) International Filing Date: 26 December 2003 (26.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/436,763 27 December 2002 (27.12.2002) US

(71) Applicant *(for all designated States except US)*: **THE JOHNS HOPKINS UNIVERSITY** [US/US]; 3400 N. Charles Street, Baltimore, MD 21218 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **KERN, Scott, E.** [US/US]; 7 Blueleaf Court, Hunt Valley, MD 21030 (US). **VAN DER HEIJDEN, Michiel, S.** [US/US]; 3120 St.Paul Street, Apt. H417, Baltimore, MD 21218 (US).

(74) Agents: **CORLESS, Peter, F.** et al.; Edwards & Angell, LLP, P.O.Box 9169, Boston, MA 02209 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report: 24 February 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/061082 A3

(54) Title: FANC GENE MUTATIONS IN CANCER

(57) Abstract: The present invention relates to methods of determining if a patient has cancer or is at increased risk of developing cancer, particularly pancreatic cancer, the method comprising testing a FANC gene for the presence of a cancer-associated coding change, wherein said presence of one or more cancer-associated coding changes is indicative of cancer or an increased risk of cancer in said patient. The invention further relates to methods of treating a patient having cancer, particularly pancreatic cancer, who has one or more cancer-associated coding changes in the FANC genes comprising the step of administering a therapeutically effective amount of a chemotherapeutic cross-linking agent.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/41127

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12Q 1/68; C07H
US CL : 435/6, 91.2; 536/23.1, 24.3
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6, 91.2; 536/23.1, 24.3

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
OMIM, STN, Rockefeller fanconi mutation database

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RISCHEWSKI et al. J Biochem. Biophys. Methods. Screening strategies for a highly polymorphic gene: DHPLC analysis of Fanconi anemia group A gene, Vol. 47 (2001) Pages 53-64	1-6
X, P	BARBER et al. Constitutional sequence variation in the Fanconi anaemia group C (FANCC) gene in childhood acute myeloid leukaemia. 2003, Vol. 121 pages 57-62.	1-6

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
17 November 2004 (17.11.2004)

Date of mailing of the international search report
07 JAN 2005

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Authorized officer
Sally Sakelaris

Telephone No. 571-272-0500

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/41127

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claim Nos.: 15,18,19,30 and 31
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
These claims are dependent from absent claims.

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-6

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/41127

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, Claims 1-6, drawn to a method of diagnosing or determining if a patient has cancer or is at increased risk of cancer, comprising testing a FANC gene for the presence of a cancer association coding change.

Group 2, Claims 7-11, drawn to a method of treating a patient having cancer through administration of a chemotherapeutic DNA cross-linking agent.

Group 3, Claim 14, drawn to a method for screening for a cancer therapeutic.

Group 4, Claims 16 and 17 drawn to FANC products including a kit and microarray.

The inventions listed as Groups 1-3 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The shared special technical feature linking Groups I-III in the present claims appears to be a method of screening the FANC gene for polymorphisms that are predictive of cancer. However, such a technical feature does not represent a contribution over the prior art, since Rishewski et al(Journal of Biochem Biophysical Methods, 2001, vol. 47, pp 53-64). teach a method of screening the Fanconia anemia group A gene for polymorphisms that are predictive of the risk of cancer. Thus, there is no special technical feature linking the recited compositions and methods of using said compositions, as would be necessary to fulfil the requirement for unity of invention.

Even further, if instead the special technical feature was deemed to be the polymorphisms in the FANC gene, again such a technical feature is not a contribution over the prior art as Demuth et al.(Euro. Journal of Human Genetics, 2000 8, 861-868) teach for example, the pathogenic, splice mutation IVS8-2A-G on page 863 in the FANCG gene.

In addition, the claimed methods of groups 1-3 have different objectives, require different process steps and require the use of different reagents. The methods of Group1 require the steps of diagnosing or determining if a patient has cancer or is at increased risk of cancer. Whereas the method of group 2 requires the steps involved in treating a patient and administering a a chemotherapeutic DNA cross-linking agent. Lastly, Group 3 includes the steps of growing cells, determining the rate of growth to indicate the potential of cancer. In addition to differences in objectives, effects, and method steps, it is again noted that the claims of the present Groups are not directed to the detection or identification of molecules having the same or common special technical feature, for the reasons discussed above.